DRUGS USED IN THE TREATMENT OF THE ALCOHOLIC

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Alcoholism is a widespread medico-social syndrome. The problem of addiction to alcohol is largely an unsolved problem, and it is uncertain how alcoholics should best be treated. It is however agreed that treatment must be adapted to the social conditions that apply in any particular locality.

The views of the World Health Organization are that (1) the treatment of alcoholics is a medical problem, and (2) the combat of alcoholism is a socio-political concern.

At Park Road Hospital the medical treatment in essence consists of (1) a brief period of inpatient hospitalization (this is usually necessary when the addiction is established), and (2) prolonged and intensive outpatient treatment on discharge, consisting mainly of group psychotherapy and private interviews. In other words, both the physical disability and the emotional disturbance require treatment. Carefully selected drug treatment makes the withdrawal phase from alcohol more tolerable and plays a particularly important role in aversion treatment of the outpatient after discharge.

DRUGS USED IN THE HOSPITAL TREATMENT OF ALCOHOLICS

The acute alcoholic episode or 'bender' is best treated in hospital, and the alcoholic on admission is usually acutely ill. It has been demonstrated that tremulousness, transient episodes of distorted sensory perception, convulsions (of the so-called acute toxic alcoholic encephalitis) and the fully developed syndrome of delirium tremens, are a closely related group of nervous symptoms following abstinence from alcohol — relative or absolute, with rapidly falling blood-alcohol levels.[1,2] These symptoms are predictable in a fairly orderly sequence and their severity depends upon the duration of the addictive drinking before the withdrawal of alcohol. Those continuously intoxicated for 48 days or more invariably develop full-blown delirium tremens in alcohol withdrawal.

(*a*) The Restless, Anxious Patient with a Tremor

A variety of drugs can be used for this stage. Lawrence[3] recommends diazepoxide ('librium') in the anxious, restless and tremulous stage, claiming effect within 30 - 90 minutes. In our experience promazine ('sparine') in doses of up to 200 mg. 4 times a day has been found to be most effective.

Addiction, particularly in alcoholics, is always a danger since they may develop psychological dependence on psychotropic drugs. Particular caution in this respect should be paid to meprobamate ('equanil'), diazepoxide ('librium'), glutethimide ('doriden') and methyprylone ('noludar'). The last two in particular create strong dependency, and in alcoholics their use should be discouraged.

Serebro[4] reports the formation of a conservation of man-power unit in Johannesburg, its aim being to minimize man-power loss through alcoholism in commerce and industry. In contrast to other approaches, this unit deals with ambulant patients, all therapy occurring while the patient is working. The patient comes in for treatment during working hours with the consent of his employer. Work is felt to be necessary for the patient's economic welfare and morale, and is in itself psychotherapeutic. All therapy and medication is under constant daily supervision and taken by the patient during his daily visits. Hypnotics and psychotropic drugs are given to the patient in one day's supply only — this acts as a control over possible addiction and prevents accidental and suicidal overdosage. In spite of a feeling that this form of treatment has several undesirable psychotherapeutic effects, it does seem to exert some form of control over habituating drugs.

(*b*) Some Views on the Treatment and Aetiology of Delirium Tremens

1. *Causes of Death in Delirium Tremens*

(*i*) *Complicating diseases.* Lung, liver, and cardiac disease, i.e. cardiac beriberi, are frequently found in delirium tremens and should always be excluded in every case by careful physical examination. Any complicating infection should be treated with an appropriate antibiotic administered systemically.

(*ii*) *Hyperpyrexia* of 104°F. or more is seen without apparent cause in some patients, who manifest convulsions, and who finally die in a state of coma and vascular collapse. Fluid requirements in such patients can be tremendous — up to 6 litres a day, and if not met there is some evidence that the prognosis is adversely affected. Hence the importance of adequate hydration with careful attention to fluid and electrolyte balance. This often necessitates intravenous administration. The mechanism of this hyperthermia is uncertain, and has been attributed to hypothalamic dysfunction.

(*iii*) A small group of patients die suddenly with no explanation. A fatty liver with resultant fat emboli to lungs and brain has been postulated.

2. *The Role of Magnesium in the Aetiology of Delirium Tremens*

Flink[5] points out the following:

(*a*) Both chronic alcoholism and delirium tremens often show low serum-magnesium levels.

(*b*) Delirium tremens often resembles the syndrome of magnesium deficiency.

(*c*) Patients with delirium tremens seem to respond better to magnesium therapy than do controls.

Wacker and Vallee[6] describe a case of magnesium-deficiency syndrome in an alcoholic corrected by treatment, yet the patient developed delirium tremens. They therefore question the validity of the above, i.e. that magnesium deficiency is often associated with, and is even a complicating factor but not the cause of, delirium tremens. Nevertheless, magnesium treatment is probably justified in delirium tremens since it has an additional sedative and anticonvulsive effect. Flink suggests 8 G. of magnesium sulphate intramuscularly, daily, in divided doses for 3 days.

3. *ACTH*

Smith[7] postulated that ACTH is beneficial in delirium tremens; the view being that in delirium tremens pituitary-adrenal insufficiency is found. Adequately controlled studies have not clearly established this, and corticotropin or adrenocorticosteroid therapy is not generally recommended in the management of delirium tremens.

4. *Sedation*

The alcoholic withdrawal state is best treated with paraldehyde, phenothiazine derivatives (promazine) or barbiturates, and treatment should ideally be begun with large enough doses of these drugs to produce sleep, tapering the dose over the next ± 7 days. Initially larger doses may be required to counteract the cross tolerance between these drugs and alcohol. (There exists an equivalence between barbiturates and alcohol — the severity of barbiturate withdrawal being ameliorated by alcohol.)

The administration of paraldehyde, 10 - 12 ml. by deep intramuscular injection (½ into each buttock) can be repeated as required, eg. t.i.d.

Friedhoff and Zitrin,[8] in comparing the effects of paraldehyde and chlorpromazine in delirium tremens, favour paraldehyde in their study. Patients with delirium tremens on paraldehyde responded on an average within 6 days, and patients on chlorpromazine on an average within 8 days. Chlorpromazine also had a slower onset of action than paraldehyde, and this is a handicap in treating hyperactive unmanageable patients.

In our experience, an initial dose of paraldehyde is often

followed by promazine (sparine) up to 200 mg. t.i.d., occasionally more. Promazine does not tend to damage the liver (hence its preference to chlorpromazine) and does not tend to have the hypotensive action of chlorpromazine.

As recovery ensues so the dosage of sedation is tapered off.

5. *Vitamins*

Thiamine and B-complex are important, especially in the presence of peripheral neuritis, Wernicke's syndrome, or the various forms of beriberi associated with alcoholism.

6. *DPN — Diphosphopyridine Nucleotide*

Research workers at Shadel Hospital in Seattle, Washington[9] report good results from the use of DPN. In 83 chronic alcoholic patients DPN greatly reduced, and in some completely removed, the craving for alcohol. Especially good results were cited in 2 patients with delirium tremens.

In the first patient convulsions, which occurred 3 - 4 times an hour, disappeared entirely after 1 hour of treatment; the delirium soon disappeared, the temperature dropped from 103 - 100°F., and the patient became mentally clear.

A second patient, who was in a state of stupor after delirium tremens cleared completely in 35 minutes and showed no further physical and mental symptoms.

DRUGS USED IN THE OUTPATIENT TREATMENT OF ALCOHOLICS

While still in hospital the patient is taught the use of 'antabuse', learning that by taking a tablet he develops a temporary inability to drink. Regular antabuse clinics are also held at weekly intervals so that new patients may experience the effects of the antabuse/alcohol reaction, and older patients may see the physical effects produced.

Two such products are in use today: (1) tetraethyl - thiuram disulphide - (antabuse, 'cronetal'), and (2) calcium carbimide ('temposil', 'dipsan').

Tetraethyl-thiuram Disulfide (Disulfiram, Antabuse, Cronetal)

It was discovered accidentally by Jacobson and Hald in Denmark, in 1947, that disulfiram combines with ethyl alcohol to produce noxious effects.

Disulfiram was therapeutically introduced under the name antabuse by Martensen and Larsen in 1948.

Disulfiram effects. Alcohol ingestion within 15 minutes of having taken disulfiram causes unpleasant and even distressing symptoms.

The face feels warm and this is followed by intense vasodilatation of the face, neck and sclerae with a rise in skin temperature.

There is intense concomitant pulsation in the face and neck, and a throbbing headache which may last as long as 6 hours.

Often breathlessness and constriction in the chest and throat are experienced and, when prominent, bronchospasm is often noted and irritation in the throat causes coughing. The pulse and respiratory rate are increased causing palpitations. Occasional nausea ensues in about ½ - 1 hour with pallor and fall in blood pressure. Shivering and a feeling of coldness is of late onset, and occurs only in severe reactions.

In general the above symptom-complex is due to an accumulation of blood acetaldehyde, formed as a result of interference with the oxidation process of the alcohol in the body.

Side-effects. Headache, a metallic taste in the mouth, drowsiness, abdominal discomfort, and impotence are known side-effects. In many early series, reports of psychotic reactions in patients on antabuse were as high as 10%.[10] This serious complication has been made less frequent (*a*) by using a lower initial dosage, and (*b*) by avoiding the use of antabuse in patients with suspected overt and latent psychosis. The exact nature of disulfiram-induced psychosis is open to dispute, and opinions range between:

(*i*) The finding of a definite organic psychosis with EEG changes. (Bennett *et al.*[11] reported electro-encephalographic changes during antabuse therapy.)

(*ii*) The view that both toxic and functional components play a part.[13]

(*iii*) The view that the process is entirely functional, owing to the removal of alcohol as a defence.[10]

Onset of antabuse psychosis. One case[11] has been reported after 3 days of treatment and another as late as 6 months after starting treatment with antabuse.[14] The average onset of psychosis is after 2 months.

Course of psychosis and treatment. The psychosis usually recedes in 1 - 3 weeks. Fordman and Zucker[13] often restarted disulfiram treatment in lower dosage without recurrence of psychotic symptoms, together with calcium carbimide. This is, however, probably an unjustifiable risk. Three types of psychosis are described by Gottesfeld *et al.*[15]: (*a*) a schizophrenic-like picture, (*b*) an acute anxiety state, and (*c*) a pseudo-toxic psychosis.

Treatment of the psychotic reaction consists of the withdrawal of disulfiram. This usually suffices, but occasional ECT is required. Treatment of the side-effects of the alcohol-disulfiram reaction consists of giving ·05 G. of anthisan intravenously. This usually has a marked effect in reducing the antabuse reaction within minutes.

Severe reactions reported with antabuse-alcohol effect. Jacobsen[16] in a series of 11,000 patients on antabuse treated over a period of 3½ years, reported 4 deaths with antabuse-alcohol reactions, owing to respiratory or circulatory collapse.

Administration and dosage. Antabuse is contraindicated and is to be avoided in patients with cardiovascular, hepatic or renal disease.

The initial dose is 2 tablets (·5 G.) followed by 1 tablet daily, *under constant medical supervision.*

Calcium carbimide (Temposil, Dipsan)

Calcium Carbimide was first described by Ferguson.[17]

Action. It inhibits one or more of the enzymes required to oxidize acetaldehyde (acetaldehyde representing one of the steps in the normal metabolism of alcohol by the body). The effects of calcium carbimide treatment are therefore due to increased blood acetaldehyde concentrations.

Alcohol-temposil reactions are *not* as severe as those found with disulfiram.

Minto *et al.*,[18] in comparing temposil with antabuse, report fewer side-effects and a quicker, although not so severe, onset of alcohol-temposil reactions.

These reactions can be rapidly minimized by intravenous injections of antihistaminics.

Temposil's main disadvantage is the increased desire to drink in the early stages of alcohol-temposil reactions, but this can be overcome by close observation of the test reactions before beginning long-term use. The recommended dosage is 100 mg. daily.

THE PSYCHOLOGICAL MEANING OF ANTABUSE TO ALCOHOLICS IN GROUP PSYCHOTHERAPY

If there is a positive reaction to the therapist, the control is accepted by the patient as though there was an oral incorporation of the therapist endowing him with superego qualities; if the patient's reaction to the therapist is negative, the antabuse becomes a focus for rebellion, i.e. it is used to express resentment, and the alcoholic may often stop taking it out of 'pique' for the therapist or as a self-punitive measure. The fact that it is prescribed by someone else and that there is considerable pressure and persuasion applied to the alcoholic to take it makes it a powerful tool for manipulating others and masking his neurotic ways; hence the patient's attitude to taking antabuse must be fully discussed in group psychotherapy.

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